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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61B 5/00 — A1

(11) International Publication Number: **WO 95/12349**

(43) International Publication Date: 11 May 1995 (11.05.95)

(21) International Application Number: PCT/NL93/00233

(22) International Filing Date: 5 November 1993 (05.11.93)

(71) Applicants *(for all designated States except US)*: AARNOUDSE, Jan, Gerard [NL/NL]; Jachtlaan 12, NL-9751 BT Haren (NL). CENTRUM VOOR BIOMEDISCHE TECHNOLOGIE RIJKSUNIVERSITEIT GRONINGEN [NL/NL]; Oostersingel 59, NL-9713 EZ Groningen (NL).

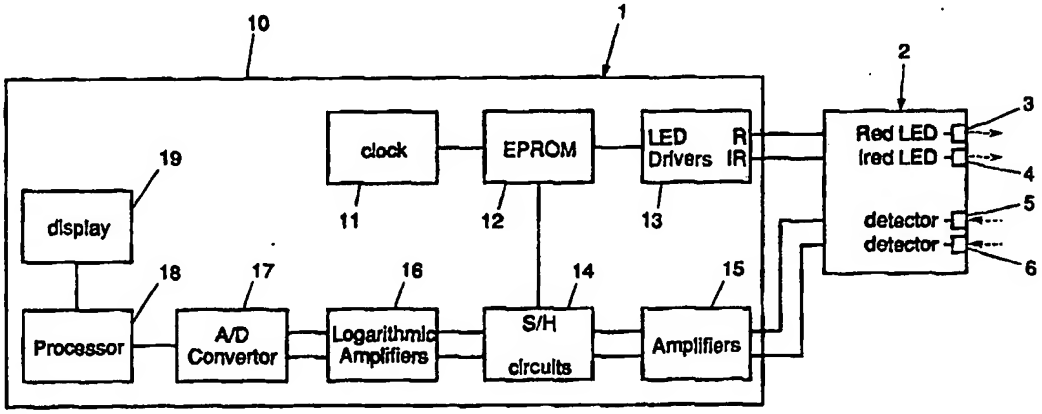
(71)(72) Applicant and Inventor: GRAAFF, Reindert [NL/NL]; Fultsemaheerd 16, NL-9736 CN Groningen (NL).

(74) Agent: SMULDERS, Th., A., H., J.; Vereenigde Octrooibureaux, Nieuwe Parklaan 97, NL-2587 BN The Hague (NL).

(81) Designated States: JP, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.

(54) Title: OPTICAL, NONINVASIVE, IN-VIVO MEASUREMENT OF PROPERTIES OF A CONSTITUENT OF A HUMAN OR ANIMAL BODY



(57) Abstract

Light of different wavelengths is introduced into a part of the body of a human or an animal, pulsatile fluctuations in the intensity of the light which has propagated through the body are measured. Intensities of light which has propagated through the body and leaves the body at different distance ranges from an entry area are measured for each of at least two wavelengths. From the light intensities estimates of properties of tissue and/or blood are calculated taking into account optical properties of the tissue and the blood influencing the intensities of light leaving the body. The method can for example be applied in pulse oximetry. A device, a probe (2) and a driver/processor (1) for use in the method according to the invention are also described.

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TITLE: Optical, noninvasive, in-vivo measurement of properties of a constituent of a human or animal body

FIELD OF THE INVENTION

The invention relates to an optical method for noninvasive, in-vivo monitoring a property of a constituent, such as blood or tissue, of a human or animal body. The invention also relates to a device, a probe and a driver/processor for carrying out that method.

BACKGROUND OF THE INVENTION

An example of a measuring method as identified above is pulse oximetry. In clinical practice, this method has become generally accepted for determining the arterial oxygen saturation (S_aO_2).

In pulse oximetry, the ratio of relative intensity fluctuations of light of different wavelengths which has passed through a portion of the body is used as an indicator for the S_aO_2. The observed fluctuations are caused by pulsatile changes of the amount of arterial blood in the tissue into which the light has been emitted. The principle underlying pulse oximetry is that the ratio of the relative intensity fluctuations at different wavelengths or wavelength ranges (generally red and infrared and therefore denoted as R/IR) is a function of the ratio of absorption coefficients of arterial blood for these wavelengths or wavelength ranges, which in turn depends on the S_aO_2. By measuring the ratio between the relative intensity fluctuations of the different wavelengths or wavelength ranges, the influence of the magnitude of the pulsations of the amount of arterial blood present in the tissue is believed to be eliminated. Empirically obtained calibration curves are used to calculate S_aO_2 estimates from the measured ratios between the relative intensity

fluctuations. In this way the influence of light scattering on R/IR is only partially taken into account.

Pulse oximetry is usually carried out by transmitting light through a relatively thin portion of the body, for example through an ear-lobe, a finger, a toe or a part of the nose.

A disadvantage of this method is that it cannot be used if suitable portions of the body cannot be reached. This problem occurs for example when it is desired to monitor the S_aO_2 of a fetus during labour. Also when the patient suffers from circulatory problems or when artefacts are caused by motion of parts of the body available for attachment of the probe, the use of transmission pulse oximetry is impaired. In particular in such situations reflectance pulse oximetry is a more appropriate technique for monitoring the S_aO_2. In this technique, the intensity of light emerging from a part of the body is measured adjacent to the area where the light has been introduced into that part of the body instead of in a position diametrically opposite to the entry area. A probe for carrying out this method comprises an emitter and a detector facing into essentially the same direction. Such a probe can for example be held against the fetal scalp during labour or to any other accessible and free part of the body, provided that pulsations of sufficient magnitude can be detected at that location.

From a publication entitled 'Design and Evaluation of an Instrument to Measure Microcirculatory Blood Flow and Oxygen Saturation Simultaneously' by Dougherty and Lowry, Journal of Medical Engineering & Technology, Vol. 16, No. 3 1992, p. 123-128, a method for noninvasively, in-vivo monitoring a property of a constituent of a human or animal body is known in which light of at least two, mutually different wavelengths or wavelength ranges is introduced through an entry area into the body. Intensities of light of each of the wavelengths or wavelength ranges leaving the body are measured in a first distance range from the entry area where the light has been

introduced into the body. Furthermore, an intensity of light of a wavelength or wavelength range leaving the body in a second distance range from the entry area where the light has been introduced into the body is measured. Finally, an estimate of the property to be monitored is determined from the measured intensities of light leaving the body in the first and second distance ranges from the entry area where the light has been introduced into the body.

According to this publication, reflectance pulse oximetry and laser Doppler flowmetry are carried out as separate independent measurements using an integrated sensor. A signal generated by a second red light (660 nm) sensitive photodiode, which is located twice as far away from the light source as a first red light (660 nm) sensitive photodiode (both photodiodes and the light source being positioned in line), is used in addition to signals generated in response to red and infrared light by the first red light sensitive photodiode respectively the infrared light sensitive photodiode. According to this publication, it was found empirically that in an S_aO_2 range between 80 and 100 %, readings from the thigh calculated with a calibration curve obtained from readings from the forehead showed a reduced bias and an improved precision if, instead of a mean intensity signal of one red light photodiode, the difference between the mean intensity signals of the first and the second red light photodiodes is used in the calculation of the S_aO_2.

There is however no empirical or theoretical evidence with respect to the universal applicability of the calibration curve, in particular at lower S_aO_2 levels.

Also the precision of the results of transmission pulse oximetry at low S_aO_2 levels is relatively low when compared with the precision at high S_aO_2 levels. In transmission pulse oximetry the achieved precision is generally limited to 1.5 to 3 % at higher S_aO_2 levels (70-100 %), while at lower levels the precision decreases and generally no measurement result is obtained if the S_aO_2 values is below 50 %.

A major factor determining the attainable precision is is the pulse size. It has been found, that partly due to relatively small pulse sizes, the precision of reflectance pulse oximetry is not as good as the reported precision when commercially available transmission pulse oximeters are used (Dassel et al., 'Reflectance Pulse Oximetry in Fetal Lambs', Pediatric Research, Vol. 31, No. 3, 1992).

Also in other noninvasive in-vivo measurement methods in which light is passed through a part of the body of a living human or animal body the problem occurs that optical properties of the tissue and fluids in that part of the body other than the properties to be measured influence the measurement result. For instance the average Doppler frequency measured during laser Doppler flowmetry, which provides an indication of relative changes in blood flow - and in clinical practice of the blood perfusion in tissue immediately below the skin - is not only determined by the blood flow, but also influenced by the optical properties of the tissue and the blood which may vary between wavelength of the emitted light, between individuals and also between different measurement locations on the body. The known empirical method described above does not provide for application in measurement techniques other than reflectance pulse oximetry.

SUMMARY OF THE INVENTION

It is an object of the invention, to provide a more precise method for estimating a property of a constituent of a part of a human or animal body from optical measurements. More in particular, it is an object of the present invention to provide such a method in which optical characteristics of the part of the body through which the detected light has propagated or from which the detected light has been reflected can be estimated and taken into account, in particular for estimating S_aO_2 levels in reflectance pulse oximetry.

According to the present invention, this object is achieved by measuring the intensities of introduced light of at least two of the wavelengths or wavelength ranges leaving the body in the second distance range from the entry area where the light has been introduced into the body, and by using the measured intensities of the light of the two or more wavelengths or wavelength ranges in the second distance range from the entry area where the light has been introduced into the body for determining an estimate of the property to be monitored.

According to the present invention, this object can also be achieved by measuring intensities of portions of the light of at least two of the wavelengths or wavelength ranges which has not been introduced into the body, and using the measured intensities of the other portions of the emitted light for determining an estimate of the property to be monitored.

In each of these two methods according to the present invention, the intensities of light of each of the at least two, mutually different wavelengths or wavelength ranges having travelled along different average path lengths through the body is detected. According to the first possibility, the position of one or more additional areas or light emitters is chosen in such a manner, that the second distance range is different from the first distance range. According to the second possibility an additional detection area is positioned in such a manner that light reaching that area has not passed through the body, i.e. the average path length through the body is zero.

Methods according to the present invention can be used for taking into account specific optical properties of the tissue and/or the blood and/or variations thereof in the calculation of estimates of the property to be monitored.

In particular, the method according to the present invention allows to differentiate between variation of the absorption coefficient and the reduced scattering coefficient of the part of the body through which the detected light has

propagated and therefore to design more universally applicable and accurate calibration procedures. In experiments by the inventor, in particular simultaneous calculation of an estimate of the reduced scattering coefficient and taking into account the estimated value thereof substantially improved the precision of estimates of the S_aO_2 obtained by reflectance pulse oximetry.

When used in combination with laser Doppler flowmetry, the method according to the present invention can provide a possibility to correct for the influence of both the absorption coefficient and the reduced scattering coefficient for the wavelength at which the laser Doppler flowmetry is performed. Thus it is possible to correct for the tendency that, at a given perfusion, the observed average Doppler frequency is larger the lower the absorption coefficient and the higher the scattering coefficient is, because the average number of scattering events each detected photon has been subjected to decreases with an increasing absorption coefficient and increases with an increasing scattering coefficient.

A further advantage of the method according to the present invention is, that also correction factors for the average penetration depth of detected light of each wavelength or wavelength range become available. This is advantageous where the assumption of a homogeneous change of the blood volume fraction leads to unacceptable inaccuracies (e.g. if pressure is applied to the probe or if measurements are taken at the scalp).

Particular advantages of the mode of the method according to the invention in which light leaving the body is detected at at least two different distance ranges from the area where the light has been introduced into the body are that also pulsatile fluctuations in the reduced scattering coefficient of arterial blood can be estimated and taken into account, so that also variations of this factor can be allowed for. Moreover, two different options to obtain estimates of

this factor are made available. A first option is to calculate the reduced scattering coefficient of arterial blood from determined or default values of the hematocrit and/or the plasma protein content. The second option is to calculate the aforementioned factor by varying it, while keeping it identical for both distance ranges, until the estimates of the property to be monitored for both distance ranges are equal or within a predetermined range of each other.

Furthermore, the availability of relations between intensities at different distance ranges for two wavelenghts or wavelength ranges provides the possibility to statistically analyze the noise contributions and to use the result thereof to obtain better estimates of R_1/IR_1 and R_2/IR_2. Moreover, an estimate of a measure of uncertainty such as a confidence interval can be obtained.

The invention can also be embodied in a device, a probe or a driver/processor adapted for use in the measuring method according to the present invention.

Particular modes and embodiments of the invention are set out in the dependent claims.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a block diagram of a device according to the present invention,

Fig. 2 is a schematic bottom view of a probe according to the present invention,

Figs. 3-5 are consecutive parts of a flow chart of an algorithm for carrying out the present invention,

Fig. 6 is a schematic side view in cross-section of a another probe according to the present invention, and

Fig. 7 is a schematic bottom view of still another probe according to the present invention.

DETAILED DESCRIPTION OF THE BEST MODE AND VARIANTS OF THE INVENTION

First, an example of a device for carrying out the method according to the present invention and then an algorithm for carrying out the method according to the invention as such will be described.

Example of a device for carrying out the method according to the invention

With reference to Fig. 1, the device generally consists of a pulse oximetry driver/processor 1 and a probe 2 which is shown in more detail in Fig. 2.

The probe 2 shown in Fig. 2, which represents the presently most preferred embodiment thereof, has a diameter of about 18 mm. It comprises a red and an infrared LED 3 respectively 4 (Cerled types CR 10 MR respectively CR 10 IR; Electronic Consulting Services, Pfaffenhofen, Germany) for emitting light at wavelengths about 660 nm respectively about 940 nm.

The probe 2 further comprises a first and a second detector in form of photodiodes 5 respectively 6 (Siemens BPW 32) of which the first detector 5 is closer to the LEDs than the second detector 6. Each of the detectors is capable of detecting light intensities at both wavelengths. The probe has an internally black housing 7 to keep disturbing light away from the entry area and the exit area of the patient's skin where light is introduced into respectively received from the part of the patient's body adjacent the probe 2. The separation wall 8 between the LEDs 3, 4 and the detectors as well as the inside of the probe 2 are also black to avoid transmission of light which has not passed through the skin from the LEDs to the detectors and to avoid re-entrance of light into the body. The detectors 5, 6 and the LEDs 3, 4 have

been fixed by filling the housing 7 with clear epoxy resin (e.g. EPOTEK 301).

The heart-to-heart distance between each of the LEDs 3, 4 and the first detector 5 is 4,8 mm. For the second detector 6 this distance is 7,4 mm. Preferably the largest LED to detector distance should not be more than 8 to 9 mm, since at greater distances apparently less reliable estimate of the optical properties of the skin and therefore of the S_aO_2 have been obtained. The maximum distance may also depend from the location at the body of the patient against which the probe is to be held. For use with animals other distances may be more suitable. The distance of the LEDs 3, 4 to each of the detectors 5, 6 is mutually equal, but may also be different for example to achieve a more equal average penetration depth of reflected light of the two wavelenghts. An equal penetration depth is particularly important when measurements are taken from parts of the body of which the structure varies substantially with the depth beneath the skin, such as the head.

The probe 2 is connected to the driver/processor 1 via a cable 9. Means for cordless communication could be provided instead.

The pulse oximetry driver analyzer 1 is to a large extent identical to existing commercially available devices.

It comprises a housing 10. In this housing 10 are provided a clock 11, which may for example provide a 2 Mhz output signal, an EPROM 12 for controlling LED drivers 13 and sample and hold circuits 14, amplifiers 15 interconnected with the detectors 5, 6 for amplifying signals received from the detectors 5 and 6. Preferably patient isolation according to customary standards is also provided.

In operation, the signals received from the amplifier 15 are demultiplexed by the sample and hold circuit 14 where also a constant signal caused by background illumination is subtracted from the received signal.

The driver/processor 1 further comprises logarithmic amplifiers 16, an analog/digital converter 17, a dataprocessor 18 and a display 19. Instead of or in addition to the display 19, a port for connecting display means such as a monitor or a plotter to the driver/processor may be provided.

In operation, the signals received from the sample and hold circuit 14 are logarithmically amplified by the logarithmic amplifiers 16 so after amplification the fluctuations are proportional to the relative fluctuations of the light intensities as detected. For determination of these relative fluctuations, signals are further amplified after high-pass filtering. The avareage intensities are derived from the unfiltered output of the logarithmic amplifiers 16. All the aforementioned signals are converted to digital values by the analog/digital converter 17, for example into 12 bit digital values each 30 ms. The digital values are inputted into the dataprocessor 18, which calculates estimates of the optical properties and of a value for the S_aO_2 on the basis of the received signals and an algorithm.

Instead of using the shown driver/processor 1, the signals can also be processed in essentially the same manner or somewhat differently using a driver/processor with another structure. Essential functional differences between the driver/processor according to the present invention and known driver/processors are, that the driver/processor according to the present invention is adapted for receiving and processing signals representing intensities of light of two or more wavelengths or wavelength ranges from two or more detectors (i.e. at least four different input signals) and programmed for calculating an S_aO_2 value which is dependent from the relation between the signals generated by the different detectors.

The processor 18 is to be programmed on the basis of functions defining the relation between on the one hand the intensities and ratios between the fluctuations of light of different wavelengths at different detectors and, on the other

hand, optical properties of the part of the body in front of the probe, tissue and/or the blood.

Monte Carlo simulations

Light propagation in turbid media - e.g. skin tissue and blood - can be characterized by the following optical characteristics: an absorption coefficient μ_a, a scattering coefficient μ_s and a phase function which is the distribution of scattering angles per scattering event.

The phase function is often characterized by the asymmetry factor g, which is defined as the average cosine of the scattering angles.

Predictions of light intensities at predetermined detectors can be obtained by carrying out Monte Carlo simulations for different values of the above-identified optical characteristics.

Monte Carlo techniques for simulating light propagation in turbid media are published in many earlier publications so the skilled person will generally be familiar with these techniques.

Nevertheless, for those who are not familiar with these techniques, the principles of Monte Carlo techniques for simulatiing light propagation in turbid media are set out below.

The intensity decay of a collimated beam of photons in a turbid medium equals the probability $p_t(z)$ that a photon has a free path with a length z:

$$p_t(z) = \frac{I(z)}{I(0)} = \exp(-\mu_a z)\exp(-\mu_s z)$$
$$= \exp[-(\mu_a + \mu_s)\, z\,] = \exp(-\mu_t z). \qquad (1)$$

I(z) is the intensity at a distance z from the location where the light enters the medium; μ_t is the transport coefficient.

The chance that a photon travels within the collimated beam to a distance between z and z + dz can be found by differentiation of Eq. (1):

$$p_t(z) - p_t(z + dz) = \mu_t \exp(-\mu_t z)dz. \quad (2)$$

These photons can be absorbed or scattered. The scattered fraction equals:

$$p_s(z) - p_s(z + dz) = \mu_s \exp(-\mu_t z)dz, \quad (3)$$

which is a fraction c - which equals μ_s/μ_t - of the photons that leave the collimated beam. This fraction c is denoted as the "albedo".

The intensity decay of a collimated beam in a turbid medium has much in common with the free path length between interactions in Monte Carlo simulations. Therefore, in Monte Carlo simulations the distribution of photon path lengths resulting from Eq. (2) is simulated by choosing random values for each free path length l_t between interactions of the photon during its course through the medium:

$$l_t = \frac{-1}{\mu_t} \ln(\varepsilon). \quad (4)$$

The Monte Carlo simulation comprises a repetition of the following sequence of steps. Firstly, a random number ε is picked between 0 and 1 to determine l_t. Secondly, a new random number is ε is picked to determine whether the photon is absorbed or scattered. Thirdly, if the photon is scattered, then a scattering angle is picked from the phase function. If the photon has been absorbed simulation of the path of that photon is terminated. If the photon has not been absorbed, the three step sequence set out above is repeated until the photon is absorbed or leaves the medium. Each time new random numbers ε are used. For reasons of efficiency, the photons may also be

deemed to be absorbed if the number of interactions is very large, e.g. more than 20.000.

To determine whether the photon has been reflected or refracted at interfaces, the Fresnel law can be used by picking a random number for each interaction to determine whether the photon is reflected or refracted.

Since Monte Carlo calculations require a substantial calculating effort, a condensed Monte Carlo simulation for semi-infinite media has been proposed in 'Condensed Monte Carlo Simulations for The Description of Light Transport' by R. Graaff et al. in Applied Optics, Vol. 32, No. 4, pages 426-434, February 1993 the contents of which is hereby incorporated by reference.

The condensed Monte Carlo simulation described in that publication essentially consists of using the results of one Monte Carlo simulation for modelling light propagation in a situation in which the albedo c, the scattering coefficient μ_s or the absorption coefficient μ_a are different from the corresponding value used in the original performed Monte Carlo simulation.

Reliable results for the same value of μ_t but for values of the albedo c smaller than the albedo c_{sim} used in the original performed Monte Carlo simulation can be obtained quickly if from the original performed Monte Carlo simulation the number of interactions within the simulated turbid medium N(i) has been stored for each photon path which has not been terminated by absorption of the photon. In that event the chance p(i) that a photon would have left a medium with an albedo c can be found for each photon using the following equation:

$$p(i) = (c/c_{sim})^{N(i)}. \qquad (5)$$

In a similar way, the average depth of all interactions of detected photons can be calculated quickly if the average depth $\langle d(1) \rangle$ of each photon path has been stored too.

If the simulated medium is semi-infinite and reflection from that medium is simulated, for each photon that has left the medium, the distance r(i) from the place of entry where that photon is deemed to have left the medium must also be available to determine the intensity in a predetermined area. If a slab has been simulated, it must furthermore be known for each photon that is deemed to have left the medium whether it is deemed to have been transmitted through the slab or to have been reflected back from the slab to determine the intensity in a predetermined area at the front or the back side of the slab.

The use of results from a Monte Carlo simulation for modelling light transport in a medium having a different phase function (characterized by the average cosine of the scattering angles g) than the phase function (characterized by g_{sim}) used in the Monte Carlo simulation is possible if similarity rules are applied, e.g. if it is assumed that if the absorption coefficients μ_a and the reduced scattering coefficients are mutually identical; i.e. if:

$$\mu_a = \mu_{a,sim}, \text{ and} \tag{6}$$

$$\mu_s' = \mu_s(1-g) = \mu_{s,sim}(1-g_{sim}), \tag{7}$$

the light distribution in the medium is the same in the simulation.

Similarity is not restricted to the range of validity of the diffusion theory, in which the reduced albedo $c' \approx 1$ ($c' \equiv \mu_s'/\mu_t'$). Similarity is also present if the reduced albedo $c' << 1$, in particular if two media containing forward scattering particles are compared within the range $0,9 < g < 1$. Similarity can therefore be applied to scattering in biological media, e.g. the human skin, provided that the simulation is also performed with a phase function where forward scattering dominates, i.e. with $g \approx 0,9$ or higher.

The results from the condensed Monte Carlo simulations are implemented in the algorithm embodied by the signal processing software for each detector 5, 6 by determining a function relating the intensities of received light to the absorption coefficient μ_a and the reduced scattering coefficient μ_s'. Preferably this is carried out by determining coefficients of polynomials by fitting the polynomial to results of Monte Carlo or condensed Monte Carlo simulations for each detector separately. These polynomials are independent from the wavelength and can for example be of the following form:

$$\ln(I) = A_0+A_1\mu_a+A_2(\mu_a)^{0,5}+A_3\mu_s'+A_4\ln(\mu_s')+A_5\mu_s'(\mu_a)^{0,5}+A_6\mu_s'^2. \quad (8)$$

From Eq. (8) derivatives

$$\xi_a = \frac{d\ln(I)}{d\mu_a} \quad \text{and} \quad \xi_s' = \frac{d\ln(I)}{d\mu_s'}$$

for each detector 5, 6 can be obtained for given values of μ_a and μ_s'. For these properties fixed values can be used, but estimates can also be obtained from in-situ measurements as is described later.

The processor 18 of a driver/processor for carrying out the method according to the invention is preferably programmed to carry out the algorithm described below with reference to Figs. 3-5.

Example of an algorithm for carrying out the method according to the invention

I. Collection of light intensity data

The step denoted with reference numeral 20 (see Fig. 3) comprises detecting and storing samples of the light intensities for red and infrared light and for both the first

and the second detector 3, 4. The samples are preferably taken with a high frequency (e.g. each 30 ms) and over a time interval which comprises at least one systole and diastole cycle. If light of the two wavelengths is emitted in an alternating sequence, values for different wavelengths of the same sample can be detected one shortly after the other. Instead of high frequency sampling, intensity values obtained at systole and diastole may be selected.

According to the presently most preferred mode of carrying out the method according to the invention for reflectance pulse oximetry, all measured intensities in a certain time-interval are stored temporarily. Subsequently, the intensity fluctuations are analyzed by means of linear regression analysis using samples of the signals over a time interval which is longer than the heart-beat cycle. The data denoted by $\ln[I_i(R)]$ and $\ln[I_i(IR)]$ are used for obtaining ratios between intensities detected at different distances from the source. The data denoted by $\Delta\ln[I_i(R)]$ and $\Delta\ln[I_i(IR)]$ are used to analyze the intensity fluctuations. The latter data are obtained after high-pass (e.g. 0.6 Hz) filtering and additional amplification of the signal (e.g. 20 times).

From the measurement results, estimates of the optical properties of the portion of the body in front of the probe 2 are calculated as is set forth below.

II. Estimation of optical properties of a part of the body

The ratio between the average intensities at the two detectors 5 and 6 are calculated from the stored values of $\ln[I_i(R)]$ and $\ln[I_i(IR)]$ as is denoted by steps 21 and 22. Subsequently, the polynomials of the structure of Eq. (8) are used inversely to calculate the reduced scattering coefficient $\mu_s'(IR)$ from the ratio between the intensities at detectors 1 and 2, for example with an assumed non-pulsatile value for $\mu_a(IR)$ of 0.035 mm^{-1} as denoted by steps 23 and 24 (see Fig. 3).

According to step 25 a fixed ratio between the reduced scattering coefficients of the total medium at the two wavelengths or wavelength ranges is assumed, for example $\mu_{s,t}'(IR) / \mu_{s,t}'(R) = 0.53$ (cf. Table 8 of 'Optical properties of human dermis in-vitro and in-vivo', R. Graaff et al., Applied Optics, Vol. 32 No. 4, February 1993, pages 435-447).

Values of the pulse independent part of the reduced scattering coefficients for infrared light can then be determined as denoted by step 26. Subsequently, the inverse algorithm using Eq. (8) is used to determine $\mu_a(R)$ from $u_s'(R)$ and $I_2/I_1(R)$ as denoted by step 27. Thus estimates of the optical properties of the medium have been obtained for both wavelengths.

III. Analysis of intensity fluctuations

Signal processing of the intensity fluctuations can be performed in several ways. The optimal choise depends on many aspects, for instance, the signal to noise ratio of the signals at each detector, and whether the LEDs generate secondary emissions at other wavelengths.

The analysis for each wavelength (λ) and each detector 5, 6 (i) is based on equations as given below. It is noted that in the equations i = 1 denotes the detector 5 closest to the light sources 3, 4 and i = 2 denotes the remote detector 6.

$$\Delta \ln[I_i(\lambda)] = \xi_{a,i}(\lambda)\ \Delta\mu_a(\lambda) + \xi_{s,i}'(\lambda)\ \Delta\mu_s'(\lambda)$$
$$= [\xi_{a,i}(\lambda) + \xi_{s,i}'(\lambda)\ F(\lambda)]\ \Delta\mu_a(\lambda) \qquad (9)$$

with

$$F(\lambda) = \frac{\mu_{s,a}'(\lambda)\ \chi - \mu_s'(\lambda)}{\mu_{a,a}(\lambda) - \mu_a(\lambda)}, \qquad (10)$$

where $\xi_{a,i}(\lambda)$ and $\xi_{s,i}'(\lambda)$ are the derivatives that are obtained in step 29 using Eq. (8) with the coefficients of the

respective detector 1 and 2 (5 and 6, respectively in Fig. 2). The terms $\mu_a(\lambda)$ and $\mu_s'(\lambda)$ are the absorption coefficient respectively the reduced scattering coefficient of the part of the body in front of the probe for wavelength λ, as determined in steps 21-28. The values $\mu_{a,a}(\lambda)$ and $\mu_{s,a}'(\lambda)$ are the absorption coefficient respectively the reduced scattering coefficient of arterial blood. The multiplier χ is optional (default value = 1); the meaning of it is discussed below.

The variations $\Delta\mu_a(\lambda)$ and $\Delta\mu_s'(\lambda)$ can also be obtained from a linear combination of $\Delta\ln[I_1(\lambda)]$ and $\Delta\ln[I_2(\lambda)]$. However, a somewhat different procedure is followed in the present algorithm.

In step 31 the absorption coefficients for oxygenated and de-oxygenated blood are calculated using input values determined in step 30 and the equations (11) and (12) set out below.

$$\mu_{a,a,oxy}(\lambda) = \frac{c_{t,Hb}}{150}\{2.12(1-f_{HbCo}-f_{Hi})\,\in_{HbO2}(\lambda) + f_{Hi}\,\in_{HbCo}(\lambda) + f_{Hi}\,\in_{Hi}(\lambda)\} + f_{a,H2O}\,\mu_{a,H2O}(\lambda) \qquad (11)$$

and

$$\mu_{a,a,de\text{-}oxy}(\lambda) = \frac{c_{t,Hb}}{150}\{2.12(1-f_{HbCo}-f_{Hi})\,\in_{Hb}(\lambda) + f_{Hi}\,\in_{HbCo}(\lambda) + f_{Hi}\,\in_{Hi}(\lambda)\} + f_{a,H2O}\,\mu_{a,H2O}(\lambda) \qquad (12)$$

In these equations (11) and (12), $\in_{Hb}(\lambda)$, $\in_{HbO2}(\lambda)$, $\in_{HbCo}(\lambda)$ and $\in_{Hi}(\lambda)$ are the extinction coefficients of de-oxyhemoglobin, oxyhemoglobin, carboxyhemoglobin, and methemoglobin, respectively. Furthermore, f_{HbCo} and f_{Hi} are the molar fractions of carboxyhemoglobin and methemoglobin in the blood, and $f_{a,H2O}$ and $\mu_{a,H2O}(\lambda)$ are the volume fraction of water in blood - for instance assumed to be $f_{a,H2O} = 0.90$ - respectively the absorption coefficient of water at wavelength λ. Finally, $c_{t,Hb}$ is the total hemoglobin content of the blood in g/L.

The total hemoglobin content $c_{t,Hb}$ as well as the fractions HbCo and Hi can be determined in step 30.

Alternatively, default values can be used for one, two or all of these three variables, for instance $c_{t,Hb} = 150$ g/L, $f_{HbCO} = 0$ and $f_{Hi} = 0$.

According to the present algorithm, the reduced scattering coefficients of arterial blood at each of the applied wavelengths only depend on the total hemoglobin content, which is obtained from step 30. To determine the reduced scattering coefficient of blood, as denoted by step 32, for instance the following relation may be used:

$$\mu_{s,a}'(660\ nm) = 10.8\ H\ (1 - H)\ (1.4 - H)\ M_{pl} \qquad (13)$$

where H is the hematocrit with $H = 0.0030\ c_{tHb}$. M_{pl} is a correction factor for the individual refractive index of blood plasma n_{pl} which is influenced by the plasma protein content. This relation can be described as follows:

$$M_{pl} = [(\frac{1.4}{n_{pl}} - 1)\ /\ [(\frac{1.4}{n_{avg}} - 1)]^{2.09},$$

where n_{avg} is the normal refractive index of blood plasma. The reduced scattering coefficient at other wavelengths can for instance be calculated using the following equation:

$$\mu_{s,a}'(\lambda_1)/\mu_{s,a}'(\lambda_2) = (\lambda_1/\lambda_2)^{-0.37}. \qquad (14)$$

R_1/IR_1 and R_2/IR_2, R_1/R_2 and IR_1/IR_2 are calculated from the light intensity data stored in step 20. The calculated ratios are stored as set out in steps 33-36. All values may be obtained in a similar way as in commercially available pulse oximeter devices, for instance by analysis of the difference between minimum and maximum. In the present algorithm the slopes obtained by linear regression analysis of the light intensity data are used as is described below. Thereby, it is possible to use the whole signal or to select the inclinations and/or declinations during the systolic parts of the

registrations, depending on the accuracy in the predicted saturation that can be obtained.

First estimates for R_1/IR_1 and R_2/IR_2 for each detector separately are obtained from the slopes $b_{R1.IR1}$, $b_{IR1.R1}$, $b_{R2.IR2}$, and $b_{IR2.R2}$ in a linear regression analysis, where the data of $\Delta\ln[I(\lambda_1)]$ and $\Delta\ln(I(\lambda_2)]$ are the independent variable by turns as denoted by step 33. Correlation coefficients and variances are also calculated.

Similarly, $b_{R1.R2}$, $b_{R2.R1}$, $b_{IR1.IR2}$, and $b_{IR2.IR1}$ are the first estimates for R_1/R_2 and IR_1/IR_2 that are obtained in step 34, where the data of $\Delta\ln[I_1(\lambda)]$ and $\Delta\ln(I_2(\lambda)]$ are the independent variable by turns. Correlation coefficients and variances are also calculated.

The correlation coefficients and variances from step 33 and 34, which also denote the 'lack of correlation' for each detector, are used in step 35 for estimation of the contributions of uncorrelated signal by each of the signals, since the correlations between the red and infrared signals are not only determined by the arterial volume fluctuations, but for instance also by noise and venous volume fluctuations, which may differ for each of the input signals. For modelling the relation between the variances and the correlation coefficients, equations of the following form can be used:

$$R^2_{R1,IR1} = (1- \frac{\delta^2_{R1}}{\sigma^2_{R1}} - \frac{\delta^2_{R1,v}}{\sigma^2_{R1}}) \; (1- \frac{\delta^2_{IR1}}{\sigma^2_{IR1}} - \frac{\delta^2_{IR1,v}}{\sigma^2_{IR1}}) \qquad (15)$$

where σ^2_{R1} and σ^2_{IR1} are the (total) variances of each signal, $\delta^2_{R1,v}$ and $\delta^2_{IR1,v}$ are uncorrelated parts of the variance caused by venous volume fluctuations, and δ^2_{R1} and δ^2_{IR2} are the uncorrelated parts of the remaining variances. The uncorrelated part of the variance can be evaluated when it is assumed, firstly, that venous volume fluctuations do not alter the uncorrelated parts of the two signals obtained with the same wavelength, secondly, that the ratio between the remaining red and infrared noise amplitudes is the same for each detector, and, thirdly, that for each wavelength the

ratio between the venous and arterial variances, for instance $\delta^2_{R1,v}/(1-\sigma^2_{R1})$, has the same value for both detectors. From these assumptions it can be concluded that the venous terms of the variance are absent in equations similar to Eq. (15) for determining the correlations between signals for the same wavelength at different detectors, as denoted by step 34. Moreover, the ratio $R^2_{R1,IR1}/R^2_{R2,IR2}$ does not depend on the venous terms in that case. The remaining terms $\delta^2_{R1}...\delta^2_{IR2}$ are solved using these assumptions.

Subsequently, better estimates for the slopes, denoted by $b'_{R1.IR1}$ etc., can be calculated as step 35 using equations of the form

$$b'_{R1.IR1} = \frac{b_{R1.IR1}}{1-\frac{\delta^2_{IR1}}{\sigma^2_{IR1}}}. \qquad (16)$$

The slopes for the values of R_1/R_2 calculated in this way are equal, $R_1/R_2 = b'_{R1.R2} = 1/b'_{R2.R1}$. This principle also applies for the slopes for IR_1/IR_2. The corrected slopes for the correlations between the red and infrared intensity fluctuations generally remain different, since none of the red and infrared signals can be considered to be independent. Therefore, the values R_1/IR_1 and R_2/IR_2 that have to be obtained are generally between both pairs of slopes, respectively. The estimate of the arterial oxygen saturation can, for instance, be calculated from the bisector between each pair of slopes.

IV. Determination of S_aO_2 from the linear regression results

a. if a homogeneous distribution of arterial volume fluctuations is assumed

Finally, the arterial oxygen saturation can be determined from the regression results. If the pulsations are

assumed to be distributed homogeneously over the medium this is performed with equations having the structure of Eq. (9):

$$R_1/IR_1 = \frac{d\ln[I_1(R)]/df_a}{d\ln[I_1(IR)]/df_a}$$

$$= \frac{\xi_{a,1}(R)\ d\mu_a(R)/df_a + \xi_{s,1}'(R)d\mu_s'(R)/df_a}{\xi_{a,1}(IR)\ d\mu_a(IR)/df_a + \xi_{s,1}'(IR)d\mu_s'(IR)/df_a} \qquad (17)$$

and corresponding equations for R_2/IR_2, R_1/R_2 and IR_1/IR_2. The differential terms represent changes in the absorption and reduced scattering coefficients caused by changes in the arterial blood volume fraction f_a:

$$d\mu_a(\lambda)/df_a = \mu_{a,a}(\lambda) - \mu_a(\lambda) \qquad (18)$$

$$d\mu_s'(\lambda)/df_a = \mu_{a,s}'(\lambda)\ \chi - \mu_s'(\lambda). \qquad (19)$$

The coefficients ξ_a and ξ_s' are obtained from step 29. Eq. (19) shows that a value for the multiplier χ different from 1 may be given to correct for deviations from the assumed values. Such deviations may for example be caused by differences between the assumed and the actual plasma protein concentrations. The multiplier χ will then have the same value for all wavelengths. The default value for χ is one (1).

The multiplier χ may also be determined from the measured values of R_1/R_2 or IR_1/IR_2. In principle both results give the same value for χ. If determined in this manner, χ corrects for deviations in the reduced scattering coefficients, but also for changes in the reduced scattering coefficient of blood during the pulsations, which may for example be caused by changes in red cell aggregation.

The only unknowns in Eqs. (17) to (19) are the absorption coefficients of the arterial blood. From Eq. (11) and (12) it follows that the absorption coefficients of blood at each wavelength are linearly related to the arterial oxygen saturation that has to be determined:

$$\mu_{a,a}(\lambda) = \mu_{a,a,de\text{-}oxy}(\lambda) + (S_aO_2/100\%)\ \mu_{a,a,oxy}(\lambda) \quad (20)$$

After substitution of Eqs. (18) to (20) into Eq. (17) the arterial oxygen saturation can be solved, since S_aO_2 is linearly related with R_1/IR_1 in Eq. (17). Substitution of the saturation into the equations for R_1/R_2, IR_1/IR_2 and R_2/IR_2 will give agreement with the measured values, provided that the value for χ is chosen correctly, and the arterial blood volume fluctuations are in fact distributed homogeneously within the part of the body from which the measurements were or are taken.

b. if a homogeneous distribution of arterial blood is not assumed

The presence of blood vessels may also influence R/IR if a fraction of the light pulsations is determined by blood within vessels of which diameters are not small compared to $1/\mu_{s,a}'(\lambda)$ or $1/\mu_{a,a}(\lambda)$. In that event the changes $d\mu_a$ and $d\mu_s'$ of the optical properties of the medium cannot be interpreted with Eqs. (18) and (19).

However, light propagation through blood contained in a vessel can be modelled by considering interaction with a blood vessel as a single interaction. Values for apparent properties for this single interaction can be obtained from (condensed) Monte Carlo simulations of diffusely illuminated cylindrical blood vessels as a function of $\mu_{a,a}d$ or $\mu_{s,a}'d$. From these simulations, the apparent chance of absorption during interaction $1\text{-}c_{a,App}$ can be calculated as well as an apparent average cosine of the scattering angle for this interaction $g_{a,App}$.

Pulsations can then me modelled as changes in the diameter of the blood vessel, which will influence the apparent absorption and reduced scattering coefficients.

It is to be taken into account, that the reduced scattering coefficient is influenced by the absorption properties of blood, whereas in the model in which the medium is assumed to be homogeneous, the reduced scattering coefficient is not influenced by the absorption properties of blood.

c. if a layered distribution of arterial volume fluctuations is assumed

Differences between the light paths of red and infrared light may introduce complications in the determination of S_aO_2 if the arterial blood volume fluctuations are a function of depth below the skin surface. In that case the results calculated with an assumed homogeneous distribution of blood pulsations will be biased. However, since the average depths of the photon paths to the detector 6 (denoted by $_2$ in the equations) remote from the light source into the body are larger than for the photon paths to the detector 5 (denoted by $_1$ in the equations) nearer to the light source, a correction algorithm can be used to allow for the differences between the average depths of the photon paths of photons reaching the different detectors 5 and 6. This can be performed by using a linear combination of the intensity fluctuations at detectors 5 and 6 for one of the wavelengths, and calculate the arterial oxygen saturation for instance from:

$$\frac{R_2/IR_2}{1+A_1\ IR_1/IR_2} = \frac{R2}{IR_2+A_1\ IR_1} = \frac{d\ln[I_2(R)]/df_a}{d\ln[I_2(IR)]/df_a+A_1 d\ln[I_1(IR)]/df_a} \qquad (21)$$

An empirically derived value of A_1, for instance $A_1 = .1.1$, can be used in the algorithms to derive S_aO_2. It is noted that Eq. (21) reduces to Eq. (17) if $A_1 = 0$. An equation similar to Eq. (21) can be given based on the values for R_1/IR_1 and IR_1/IR_2 with an empirical value for A_2, which differs from the value for A_1. The saturations derived with both equations

will be the same, if the value for χ has been estimated correctly. Therefore, the results can also be used to derive a value for χ or to obtain a second estimate for this multiplier as will be described below.

Another option - provided for in the algorithm shown in the drawings - is to determine the values for A_1 and/or A_2 from (condensed) Monte Carlo simulation data, based on the principle that the average depth from which the signal contributions occur should be equal for both wavelengths. To derive the average depths for each detector from condensed Monte Carlo simulations it is necessary that the average depth for each photon path, d[i] has been stored. The average depth of all detected photons as a function of μ_a and μ_s' can then be obtained from

$$\langle D \rangle = \frac{\langle d[i]\ p[i]\ N[i] \rangle}{\langle p[i]\ N[i] \rangle}. \qquad (22)$$

The number of interactions N[i] has been inserted in the weight function to correct for the size of the contribution which is proportional to the path length, or N[i]. For the use of <D> in the determination of A_1 the results for <D> can be described by polynomials which have been designed in a similar way as Eq. (8) by fitting the Monte Carlo data of <D> as a function of μ_a and μ_s' for each detector. This method is applied in step 37.

In step 38 the values for A_1 and A_2 are derived. The correction for the influence of depth dependent fluctuations of the arterial volume fraction for the red signal at the second detector 6 is obtained with

$$\langle D_2(R) \rangle = \frac{\langle D_2(IR) \rangle + A_1\ IR_1/IR_2\ \langle D_1(IR) \rangle}{1 + A_1\ IR_1/IR_2}, \qquad (23)$$

which gives the value of A_1. A similar equation can be solved for the red light received at the detector 5 nearest to the light source which gives A_2.

With the obtained values for A_1 and/or A_2 the oxygen saturation(s) are derived as is denoted by step 40. For the results of R_2/IR_2 and IR from step 36 the combination of Eqs. (17) and (23) yields

$$\frac{R_2/IR_2}{1 + A_1\ IR_1/IR_2} = \frac{\xi_{a,2}(R)\ d\mu_a(R)/df_a + \xi_{s,2}'(R)\ d\mu_s'(R)/df_a}{[\xi_{a,2}(IR)+A_1\xi_{a,1}(IR)]d\mu_a(IR)/df_a+[\xi_{s,2}'(IR)+A_1\xi_{s,1}(IR)]d\mu_s'(IR)/df_a} \quad . \quad (24)$$

After substitution of Eqs. (18) to (20) into Eq. (24) the relation between S_aO_2 and the lefthand term in Eq. (24) is found. S_aO_2 is calculated using this relation in step 40. Substitution of the saturation into a similar equation based on R_1/IR_1 and the corresponding constant A_2 will give agreement with the measured values provided that the value for χ is chosen correctly. The initial value of χ can be a fixed default value or be specified - for example obtained from Eq. (19) - as denoted by step 39.

In step 41 it is checked whether the S_aO_2 calculated with A_2 is within a predetermined tolerance range about the S_aO_2 value calculated for A_1. If the value calculated for A_2 is outside that tolerance range, then at step 43 the value of χ is varied, the new value is read in step 39 and the calculations of step 40 are repeated with that new value of χ. The cycle of steps 38-41 and 43 is repeated until the value calculated with A_2 is within the specified tolerance range. Then the S_aO_2 estimate is displayed with the corresponding measure of uncertainty (step 42).

Alternatively, the most likely value for S_aO_2 can be calculated from the two estimated values for the S_aO_2 and the uncertainties in these properties.

Alternative modes and embodiments of the invention

Within the framework of the present invention many other alternatives will be apparent to the skilled person, both

regarding the hardware for carrying out the method as regarding modes for carrying out the method.

In the shown algorithm many steps may be carried out in a different order. For example the step 37 in which the average penetration depth is determined may be carried out immediatley after the μ_a and μ_s' have become available from step 28. Furthermore, for example steps 33 to 36, in which the relations between relative fluctuations at different distance ranges and different wavelengths or wavelength ranges are analyzed, can be carried out immediately after the measuring step 20 and before analysis of the avarage intensities in steps 21 to 29.

It is also possible to leave out one or more steps. For example where the direct comparison of light intensities detected at different detectors is not reliable - this occurs for example if measurements are taken from the fetal scalp during labour, because of the possible presence of hair, meconium, and vernix in front of one or more of the detectors - it is generally more reliable to use assumed values for μ_a and μ_s' so the steps 21-28 can be replaced by entering assumed or default values. It is noted that the measurement of relative fluctuations is not affected by the presence of obstacles in front of one or more of the detectors as long as sufficient light reaches the detectors. Measurement of the hematocrit and hemoglobin fractions will generally not appear opportune where normal values can be expected. In such situations steps 30 and 31 can be replaced by enetering assumed or default values.

In Fig. 6 another probe according to the invention,is shown in a position against a body 110. This probe comprises two LEDs 103, 104, a first detector 105 and a second detector 106. The second detector is positioned at the side of the LEDs facing away from the side of the probe which is to be held against the skin. Connection 109 comprises individual connections for each detector 105, 106 and for each LED 103, 104. Instead of for determining the ratio between light at

different distances from the source, this probe is adapted for determining the ratio between light which has propagated through the skin and light which has reached the detector 106 without propagating through the skin. Relations between that ratio and values of μ_a and μ_s' can be provided, so μ_a and μ_s' can be determined for each wavelength using these ratios. These ratios can also be used in addition to ratios between light intensities at different distance ranges from the light source, so that less assumptions are needed and more variations of optical properties can be taken into account.

In Fig. 7 still another probe according to the present invention is shown. In this probe two detectors 204 and 205 are provided. Detector 204 is adapted for detecting red light and detector 205 is adapted for detecting infrared light. For emitting red light LEDs 201, 202 at diferent distances from the detector 204 are provided. For emitting infrared light LEDs 200, 203 at diferent distances from the detector 205 are provided. Alternating operation of on the one hand the LEDs 202, 203 close to the detectors 204, 205 and, on the other hand, the LEDs 200, 201 remote from the detectors 204, 205, provides the possibility to measure intensities of light leaving the body at different distances from the area where the light has been introduced into the body.

CLAIMS

1. A method for noninvasively, in-vivo monitoring a property of a constituent of a human or animal body comprising the actions of:

introducing light of at least two, mutually different wavelengths or wavelength ranges through at least one entry area into the body,

measuring intensities of light of each of said wavelengths or wavelength ranges leaving the body in a first distance range from the entry area where the light has been introduced into the body,

measuring an intensity of light of a wavelength or wavelength range leaving the body in a second distance range from the entry area where the light has been introduced into the body, and

determining an estimate of the property to be monitored from the measured intensities of light leaving the body in said first and second distance ranges from the entry area where the light has been introduced into the body,

characterized by:

measuring the intensities of introduced light of at least two of said wavelengths or wavelength ranges leaving the body in said second distance range from the entry area where the light has been introduced into the body, and

using said measured intensities of the light of said at least two wavelengths or wavelength ranges in said second distance range from the entry area where the light has been introduced into the body for determining an estimate of the property to be monitored.

2. A method according to claim 1 in which, for each of at least two of said wavelengths or wavelength ranges, the ratio between intensities of the light leaving the body in said first and second distance ranges from the entry area is calculated.

3. A method according to claim 1 or 2 in which, for a number of samples and each of at least two of said wavelengths or wavelength ranges, ratios between relative intensity fluctuations of the light leaving the body in said first and second distance ranges from the entry area are calculated, noise contributions are determined and ratios are corrected using these noise contributions.

4. A method according to any one of the preceding claims in which an estimate of the reduced scattering coefficient of arterial blood and changes thereof are calculated from a ratio of relative fluctuations of light of the same wavelength or wavelength-range at different distance ranges from the area where the light has been introduced into the body.

5. A method according to any one of the preceding claims in which a common multiplier representing changes in the reduced scattering coefficient of blood in estimates of the S_aO_2, obtained from measurements at different distance ranges from the entry area where the light has been introduced into the body, is varied until a value for this multiplier is found for which one of these estimates is within a predetermined tolerance range around the other estimate.

6. A method for noninvasively, in-vivo monitoring a property of a constituent of a human or animal body comprising the actions of:

emitting light of at least two, mutually different wavelengths or wavelength ranges,

introducing at least a portion of said light through at least one entry area into the body,

measuring intensities of light of each of said wavelengths or wavelength ranges leaving the body in a distance range from the entry area where the light has been introduced into the body, and

using said intensities measured at said distance range from the entry area where the light has been introduced into the body for determining an estimate of the property to be monitored,

characterized by:

measuring an intensity of other portions of the light of at least two of said wavelengths or wavelength ranges which have not been introduced into the body, and

using the measured intensities of said other portions of the emitted light for determining an estimate of the property to be monitored

7. A method according to claim 6 in which, for each of at least two of said wavelengths or wavelength ranges, the ratio between intensities of the light leaving the body in said distance range from the entry area and said other portion of light is calculated.

8. A method according to any one of the preceding claims in which relations between light intensities detected at each of said different areas and estimates of optical properties of the body are provided and at least one of said optical properties is determined by comparing the intensities of light of the same wavelength leaving the body at different distance ranges from the area where the light has been introduced into the body.

9. A method according to claim 8 in which these relations are provided in form of polynomials of which variables represent the optical properties.

10. A method according to claim 8 in which these relations are provided in form of sets of coordinates in an at least three dimensional space.

11. A method according to any one of the preceding claims in which correction factors for the average penetration depth of light leaving the body in each of said distance ranges from the area where the light has been introduced into the body are provided for each wavelength or wavelength-range.

12. A method according to any one of the preceding claims in which the light of which the intensities are measured leaves the body through surfaces facing in essentially the same direction as the entry areas through which that light has been introduced into the body.

13. A device for carrying out a method according to any one of the preceding claims comprising a probe (2) and a pulse oximetry driver/processor (1) connected to that probe,

said probe (2) comprising cooperating light emitting means (3, 4; 103, 104; 200, 201, 202, 203) and light detector means (5, 6; 105, 106; 204, 205) positioned at different mutual spacings, said light emitting means (3, 4; 103, 104; 200, 201, 202, 203) and said light detector means (5, 6; 105, 106; 204, 205) being adapted for emitting respectively receiving light of at least two, mutually different wavelengths or wavelength ranges, and

said driver/processor (1) comprising signal processing means (15-18) adapted for determining an estimate of a property to be monitored from signals representing light intensities of at least two wavelengths or wavelength ranges received from light emitting means (3, 4; 103, 104; 200, 201, 202, 203) differently spaced from the detector means (5, 6; 105, 106; 204, 205) from which the signals are received, means for communicating signals from the light detector means (5, 6; 105, 106; 204, 205) to the signal processing means (15-18), and display means (19) or a port for connecting such display means connected to said signal processing means (15-18).

14. A probe for use in the method according to any one of the claims 1-12 comprising cooperating light emitting means (3, 4; 103, 104; 200, 201, 202, 203) and light detector means (5, 6; 105, 106; 204, 205) positioned at different mutual spacings, said light emitting means (3, 4; 103, 104; 200, 201, 202, 203) and said light detector means (5, 6; 105, 106; 204, 205) being adapted for emitting respectively receiving light of at least two, mutually different wavelengths or wavelength ranges.

15. A probe according to claim 14 in which the light detector means comprise detectors (5, 6) or sets of detectors positioned at mutually different distances from the light emitting means (3, 4), each detector of set of detectors being connected to an individual associated communication line.

16. A probe according to claim 14 in which the light emitting means comprise light emitters (200, 201, 202, 203) or sets of light emitters positioned at mutually different distances from the light detector means (204, 205), each emitter (200, 201, 202, 203) or set of emitters being connected to an individual associated power supply line for alternating operation of that emitter (200, 201, 202, 203) or set of emitters.

17. A probe according to claim 14 in which the light detector means comprise detectors (105, 106) or sets of detectors positioned in mutually different directions from the light emitting means (103, 104) such that at least one of said detectors or sets of detectors is positioned for directly receiving a portion of the light emitted by the light emitting means, each detector or set of detectors being connected to an individual associated communication line.

18. A probe according to any one of the claims 14-17, in which the emitting surfaces of light emitting means (3, 4; 103, 104; 200, 201, 202, 203) and the receiving surfaces of the light detectors (5, 6; 105, 106; 204, 205) are facing in essentially the same direction.

19. A pulse oximetry driver/processor for use in the method according to one of the claims 1-12, comprising

signal processing means (15-18) adapted for determining an estimate of a property to be monitored from signals representing light intensities of at least two wavelengths or wavelength ranges received from light emitting means (3, 4; 103, 104; 200, 201, 202, 203) differently spaced from the detector means (5, 6; 105, 106; 204, 205) from which the signals are received,

means for communicating signals from the light detector means (5, 6; 105, 106; 204, 205) to the signal processing means (15-18), and

display means (19) or a port for connecting such display means connected to said signal processing means (15-18).

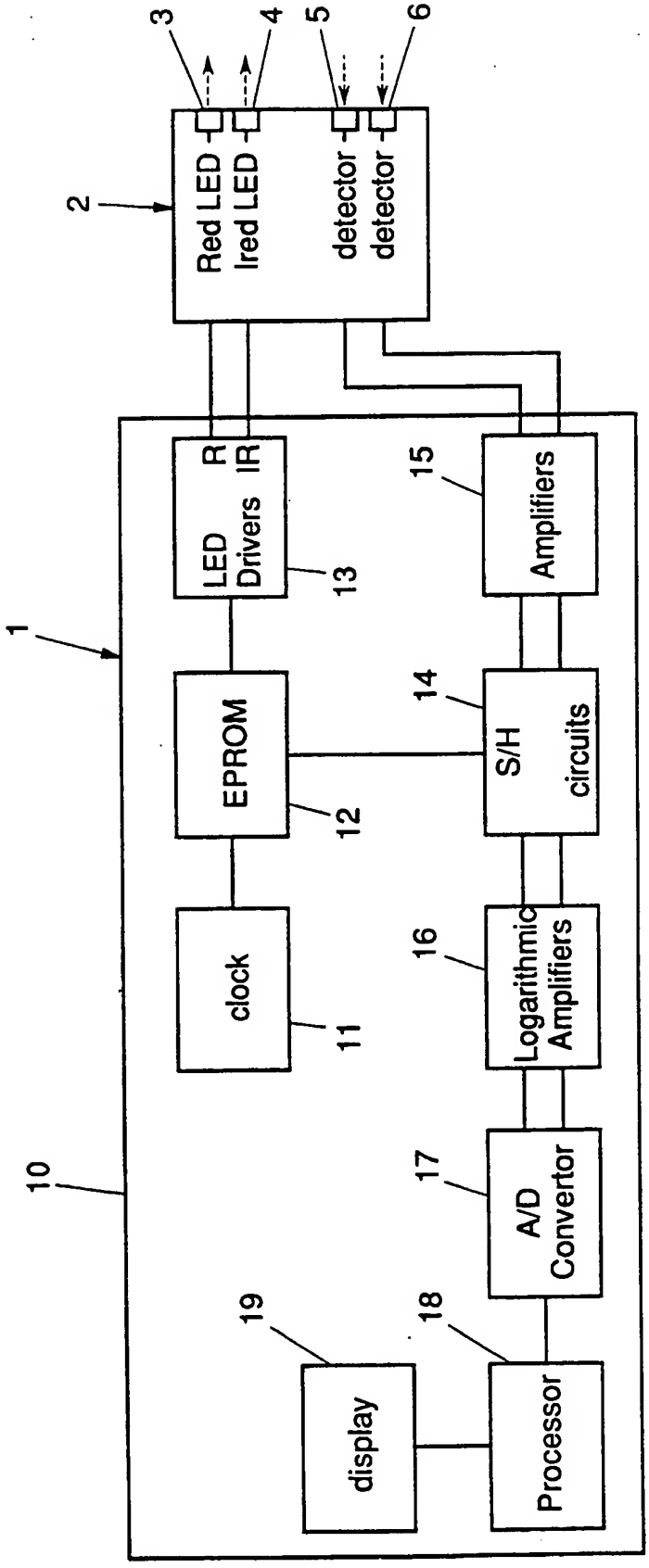
3
4
5
6
2
Red LED
Ired LED
detector
detector
1
R
IR
LED Drivers
13
15
Amplifiers
EPROM
12
14
S/H circuits
clock
11
16
Logarithmic Amplifiers
10
17
A/D Convertor
19
18
display
Processor

FIG. 1

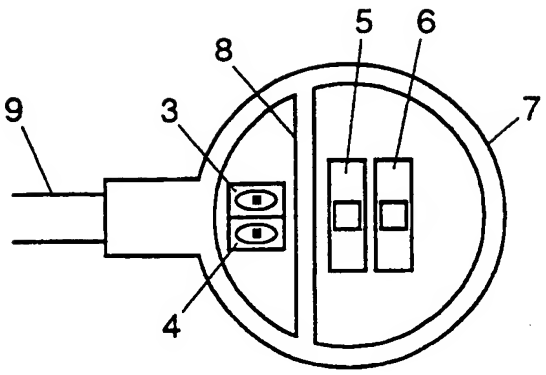

FIG. 2

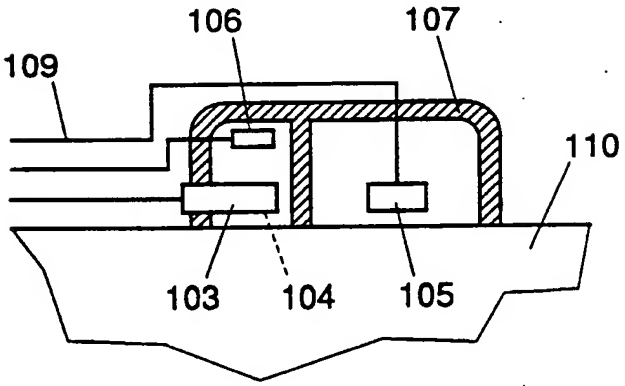

FIG. 6

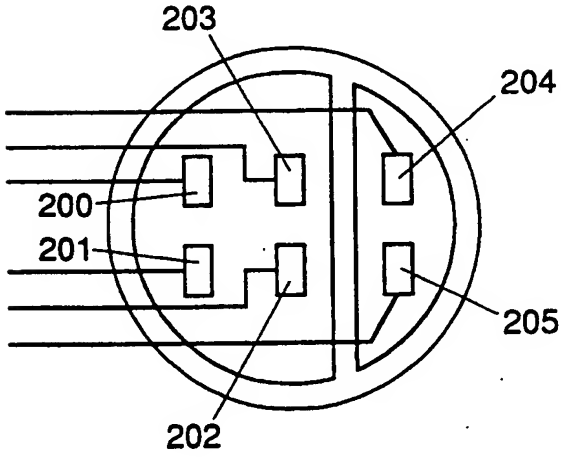

FIG. 7

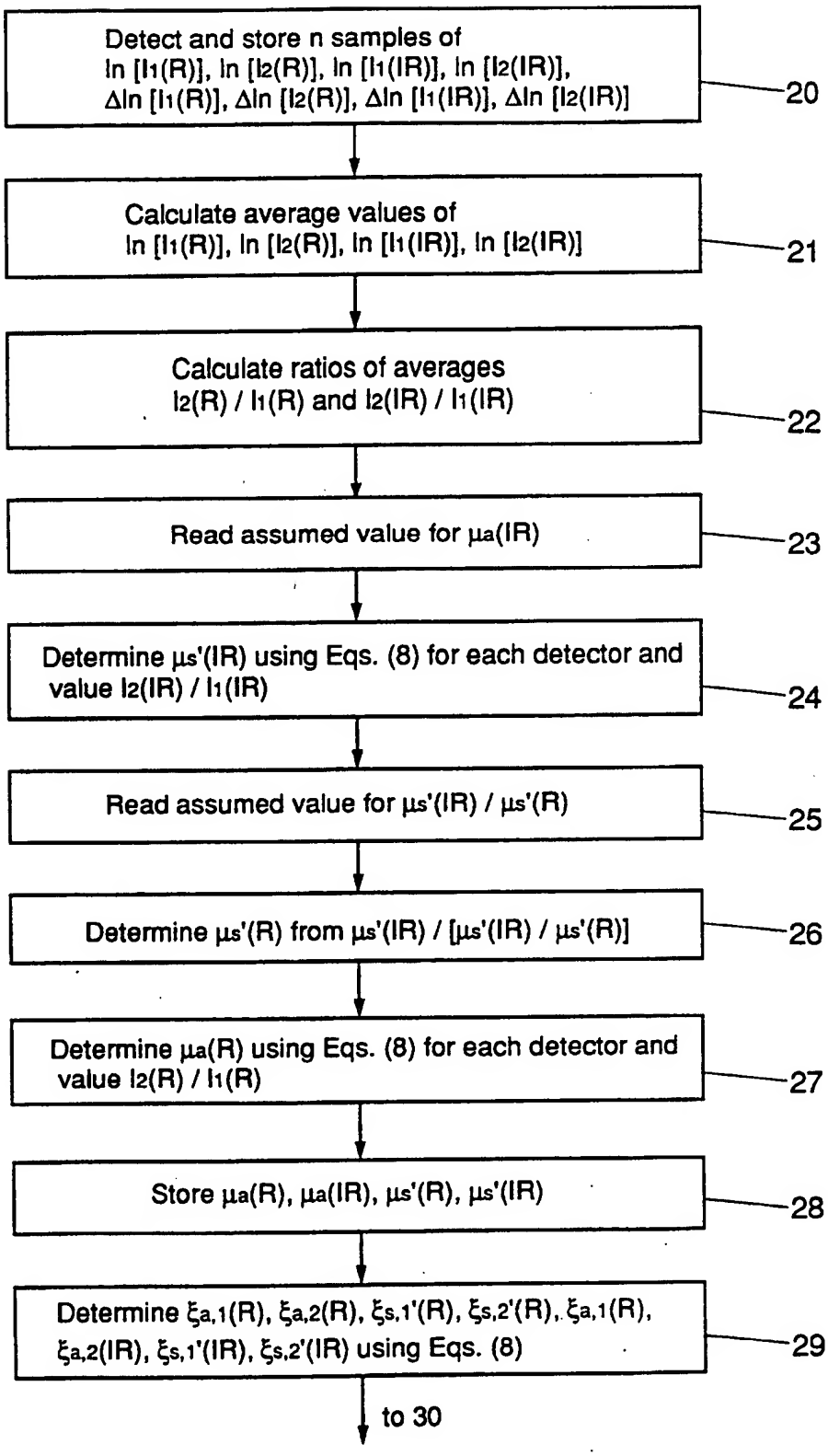
Detect and store n samples of ln [I1(R)], ln [I2(R)], ln [I1(IR)], ln [I2(IR)], Δln [I1(R)], Δln [I2(R)], Δln [I1(IR)], Δln [I2(IR)]
20
Calculate average values of ln [I1(R)], ln [I2(R)], ln [I1(IR)], ln [I2(IR)]
21
Calculate ratios of averages I2(R) / I1(R) and I2(IR) / I1(IR)
22
Read assumed value for μa(IR)
23
Determine μs'(IR) using Eqs. (8) for each detector and value I2(IR) / I1(IR)
24
Read assumed value for μs'(IR) / μs'(R)
25
Determine μs'(R) from μs'(IR) / [μs'(IR) / μs'(R)]
26
Determine μa(R) using Eqs. (8) for each detector and value I2(R) / I1(R)
27
Store μa(R), μa(IR), μs'(R), μs'(IR)
28
Determine ξa,1(R), ξa,2(R), ξs,1'(R), ξs,2'(R), ξa,1(R), ξa,2(IR), ξs,1'(IR), ξs,2'(IR) using Eqs. (8)
29
to 30

FIG. 3

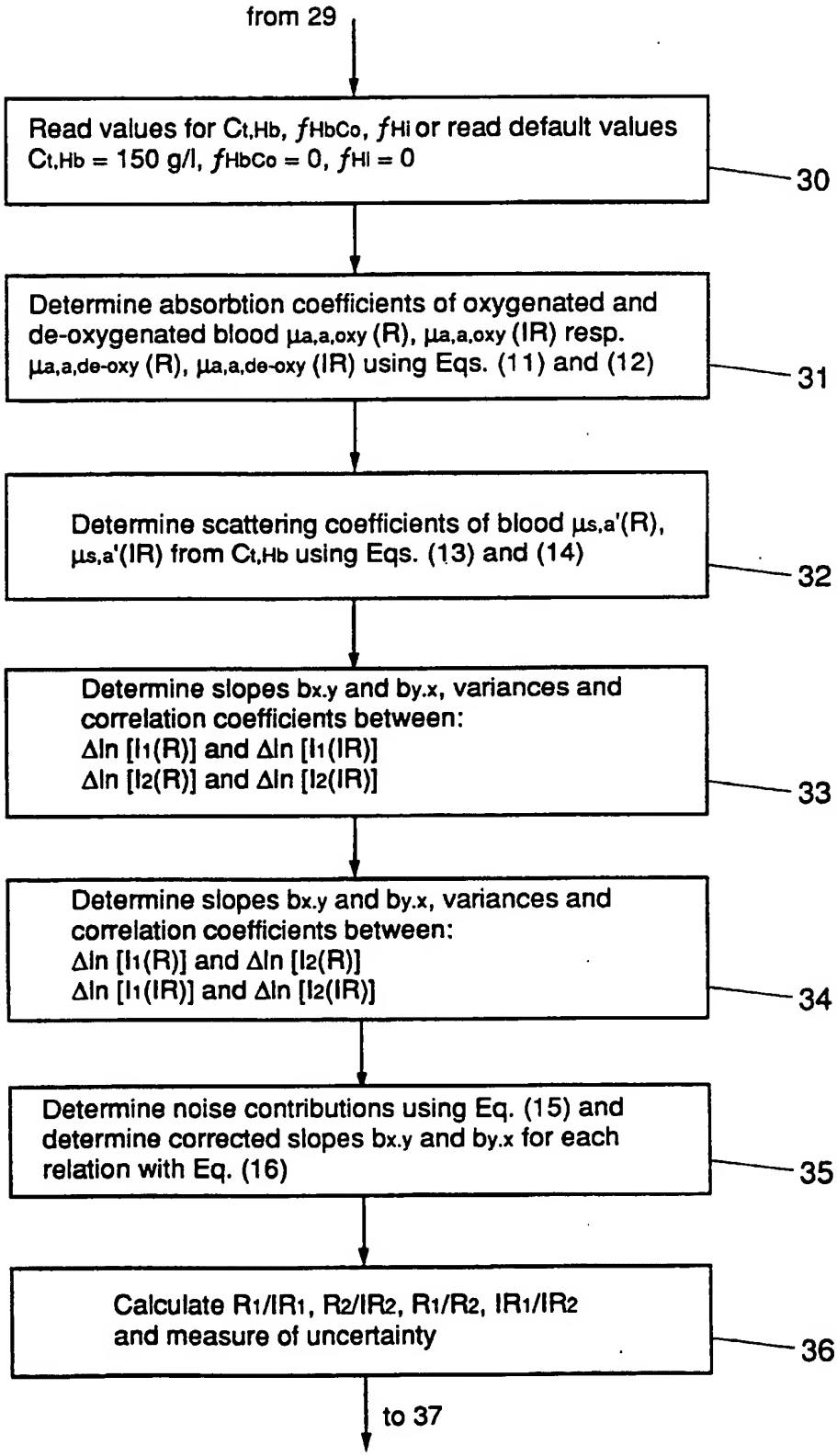
from 29
Read values for $C_{t,Hb}$, f_{HbCo}, f_{HI} or read default values $C_{t,Hb}$ = 150 g/l, f_{HbCo} = 0, f_{HI} = 0
30
Determine absorbtion coefficients of oxygenated and de-oxygenated blood $\mu_{a,a,oxy}$ (R), $\mu_{a,a,oxy}$ (IR) resp. $\mu_{a,a,de\text{-}oxy}$ (R), $\mu_{a,a,de\text{-}oxy}$ (IR) using Eqs. (11) and (12)
31
Determine scattering coefficients of blood $\mu_{s,a'}$(R), $\mu_{s,a'}$(IR) from $C_{t,Hb}$ using Eqs. (13) and (14)
32
Determine slopes $b_{x.y}$ and $b_{y.x}$, variances and correlation coefficients between:
$\Delta \ln [I_1(R)]$ and $\Delta \ln [I_1(IR)]$
$\Delta \ln [I_2(R)]$ and $\Delta \ln [I_2(IR)]$
33
Determine slopes $b_{x.y}$ and $b_{y.x}$, variances and correlation coefficients between:
$\Delta \ln [I_1(R)]$ and $\Delta \ln [I_2(R)]$
$\Delta \ln [I_1(IR)]$ and $\Delta \ln [I_2(IR)]$
34
Determine noise contributions using Eq. (15) and determine corrected slopes $b_{x.y}$ and $b_{y.x}$ for each relation with Eq. (16)
35
Calculate R_1/IR_1, R_2/IR_2, R_1/R_2, IR_1/IR_2 and measure of uncertainty
36
to 37

FIG. 4

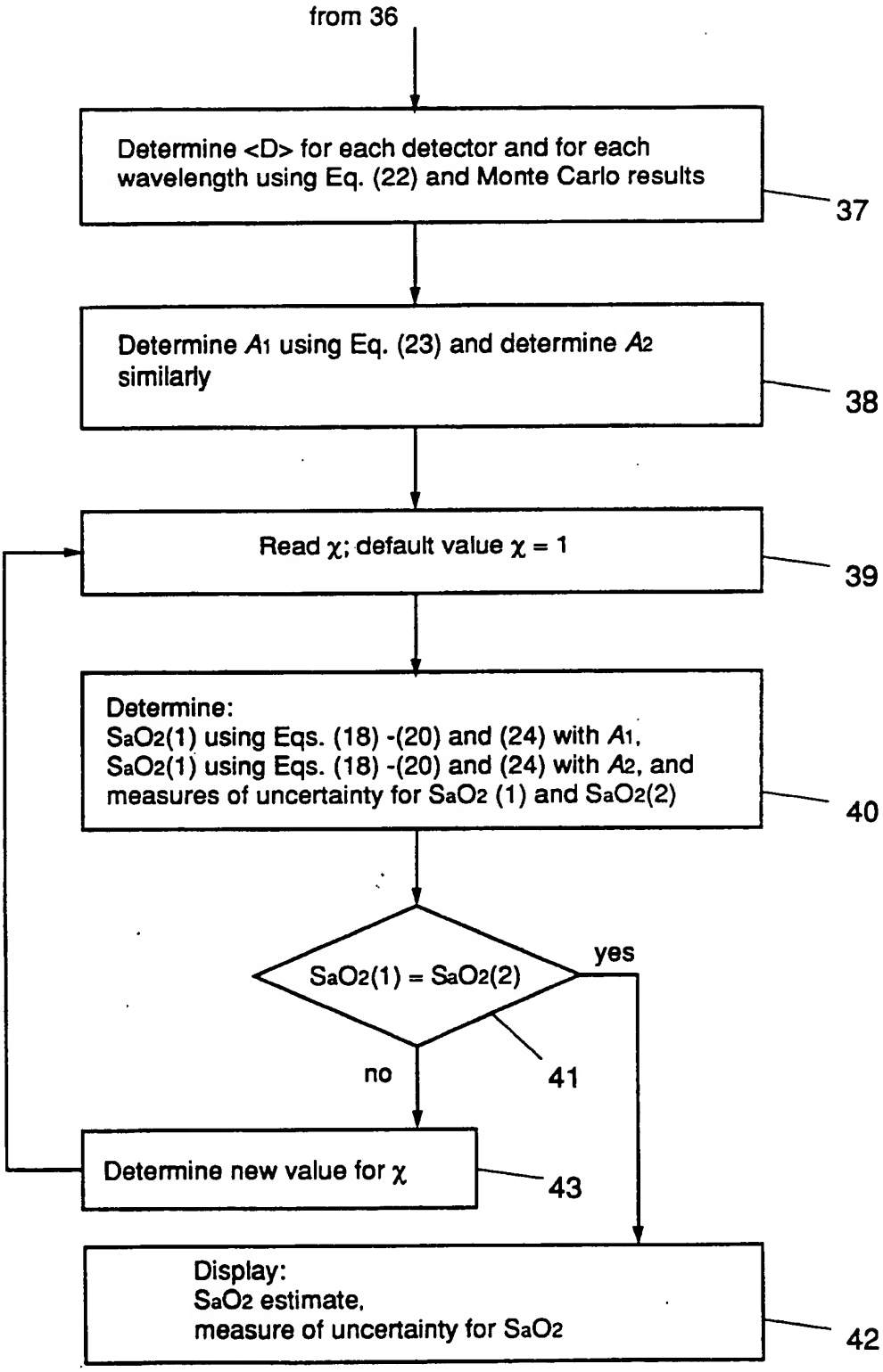
from 36
Determine <D> for each detector and for each wavelength using Eq. (22) and Monte Carlo results
37
Determine A_1 using Eq. (23) and determine A_2 similarly
38
Read χ; default value $\chi = 1$
39
Determine:
$SaO_2(1)$ using Eqs. (18) -(20) and (24) with A_1,
$SaO_2(1)$ using Eqs. (18) -(20) and (24) with A_2, and
measures of uncertainty for SaO_2 (1) and $SaO_2(2)$
40
$SaO_2(1) = SaO_2(2)$
yes
no
41
Determine new value for χ
43
Display:
SaO_2 estimate,
measure of uncertainty for SaO_2
42

FIG. 5

INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/NL 93/00233

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61B5/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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Y	see the whole document	16,17
Y	EP,A,0 442 011 (HEWLETT-PACKARD GMBH) 21 August 1991 see page 8, line 54 - page 11, line 40; figures 1-10	16
X	EP,A,0 280 986 (SUMITOMO ELECTRIC INDUSTRIES LTD.) 7 September 1988	6
Y	see the whole document	17

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
27 July 1994	25.08.94

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Hunt, B

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INTERNATIONAL SEARCH REPORT

Inten. .nal Application No
PCT/NL 93/00233

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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A	JOURNAL OF MEDICAL ENGINEERING AND TECHNOLOGY, vol.16, no.3, May 1992 pages 123 - 128 G.DOUGHERTY ET AL. 'Design and evaluation of an instrument to measure microcirculatory blood flow and oxygen saturation simultaneously' cited in the application see page 124 - page 126, paragraph "Instrument design"	1,6
X	EP,A,0 380 664 (TERUMO KABUSHIKI KAISHA) 8 August 1990 see page 11, line 4 - page 14, line 20; figures 1-22	1-4,19
A	EP,A,0 374 844 (OTSUKA ELECTRONICS CO. LTD.) 27 June 1990 see abstract; figures 1-12	1,6

1

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter al Application No
PCT/NL 93/00233

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